

In re Application of:
Frudakis and Shriver
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Filed: August 19, 2003
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Attorney Docket No.: DNA1170-2

REMARKS

Claims 2, 7, 10-11, 13-14, 17-20, 23, 25-28, 33-36, 38, 46 and 598-82 have been canceled without prejudice or disclaimer. Claims 1, 24, 31, 39-42, 45, 48, 50-51, 53-54 and 56-57 have been amended. Subsequent to the entry of the present amendment, claims 1, 3-6, 8-9, 12, 15, 16, 21, 22, 24, 29-32, 37, 39-45, and 47-58 are pending and at issue. These amendments and additions add no new matter as the claim language is fully supported by the specification and original claims.

I. Amendment to the Claims

Claim 1 has been amended to clarify that the method detects SNPs and for clarity of language and to correct technical errors. The limitations of dependent claim 7 have also been incorporated into claim 1.

Claim 31 has been amended to clarify that the method detects SNPs and for clarity of language and to correct technical errors. The limitations of dependent claim 38 have also been incorporated into claim 31.

Claims 24, 39-42, 45, 50, 52-54 and 56 have been amended for clarity of language and to correct technical errors.

As such, the amendments to the claims are fully supported by the specification and claims as filed and therefore add no new matter.

II. Restriction Requirement

Regarding the Restriction Requirement, the Examiner's comments are noted. For at least the reasons stated before in the Reply filed November 21, 2005, Applicant's respectfully request reconsideration and withdrawal of the Restriction Requirement.

The Examiner states that "Applicants traverse the species election...on the ground that individual markers are from a single gene, and therefore are related and should be examined together." Office Action at 3.

Applicants submit that the Examiner misstates or misunderstands Applicants arguments and therefore wish to clarify and elaborate the basis for traversal of November 21, 2005, for the record.

Regarding the number of sequences that may be examined in a single application, Applicants note that the administrative authority to impose a Restriction Requirement is based on the statutory right to a patent for a *single* invention. It is not, as the Examiner suggests, authorized as a matter of administrative convenience to limit the search that must be performed by the Patent Office.

The rules as applied to sequences contemplate that composition claims directed to single gene encoding a protein are considered a single invention. Composition claims directed to a second gene encoding a second protein are considered a second invention. Thus, the statutory authority to impose a Restriction Requirement in such cases flows from the consideration that the two compositions are different inventions. The framework upon which this basis for Restriction

contemplates that all polynucleotides are genes that encode proteins. This is far from reality, as is well known in the art.

In this case, the claims are directed to a method – not a composition. The method involves detecting genomic information and drawing an inference based on the information detected. The information resides in structural, non-coding regions of the genome that share the property of marking or acting as a tracer for the ancestry of the chromosomes of an individual. The presently claimed invention specifically excludes genes that are linked to the trait that is to be inferred. Thus, the present invention does not lie in the individual sequences themselves, but in the detection of a group of species from a genus of ancestry informative structural markers of the genome that is comprised of individual AIMs, which are located in non-coding regions, and dispersed throughout the genome. Indeed, an essential feature of the invention is the detection of AIMs that are not located in genes or linked to genes, particularly genes linked to an ancestry-associated trait. Accordingly, the application of the paradigm under which the Restriction is based, is fundamentally flawed as applied to the present invention.

Furthermore, the assertion that a single claimed method is really a multitude of methods, each detecting a different AIM, is equally flawed. The present invention puts together the pieces of a puzzle (ie, detection of AIMs) to reveal a picture of the ancestry of an individual. If only a few pieces are available, the picture is less clear, but some information can be discerned. Nevertheless, arbitrarily limiting the number of pieces that can be included in the invention eviscerates the value of the invention by reducing the clarity and resolution that can be achieved

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when all the pieces are available. The chemical structure of the individual sequences as potential coding regions is not relevant to the method any more than the color of a screw is relevant to a method for assembling a device held together by the screws. Would the method of assembling the device be any less a single method because the screws were of different size or shape?

Would a method of retrieving bits of data from a computer be any less a single and unitary method if there were 1 bit of data that could be retrieved or thousands? Applicant submit that it would not, and neither is the present method any less a single and unitary method that should not be arbitrarily restricted based on the individual AIMS that can be detected as a method for making an inference.

Accordingly, reconsideration and withdrawal of the Restriction Requirement as applied to SEQ ID NOs:1-331 is respectfully requested.

Notwithstanding the requested reconsideration, Applicants reserve the right to examination of a reasonable number of species in addition to the those elected for examination purposes when the generic claims are found allowable. *See* MPEP 821.04(a).

Moreover, Applicants submit that in view of the present amendments and remarks, the generic claims are allowable and claims directed to the remaining species are entitled to rejoinder.

Accordingly, withdrawal of the Restriction Requirement and rejoinder as applied to SEQ ID NOs:1-331 is respectfully requested.

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III. Priority

According to the Examiner, "Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date: U.S. applications 10/156,995, filed 5(28/200 and 10/188,359, filed 7/01/2002 and PCT/US02/38345, filed 11/26/2002, for claims 1, 3-5, 7-9,24, 29-32, 38-45, and 47-59." Office Action at p. 3-4. The Office Action states, "[i]f applicants desire benefit of these applications, applicant is invited to point to specific support by page and line number for each limitation of instant claims in the provisional applications mentioned above. *Id.* at 4.

Applicants respectfully submit that the Examiner has misstated the law, rule and guidance on which the claimed priority is based. Applicants note that the present application claims priority to US. Application Nos. 10/156,995, and 10/188,359 and to International Application No. PCT/US02/38345 as Continuations-in-Part (CIP). By definition, a CIP builds upon and adds new matter to the parent from which priority is derived. *See* MPEP 201.08.

Applicants are not aware of any requirement to show the priority for *each and every* limitation of the claims of a CIP in a parent application as that would contravene the intention to allow the introduction of new matter into a CIP application. *See* 37 CFR §1.53(b)(2), stating that a continuation in part "may disclose and claim subject matter not disclosed in the prior application."

The Examiner is invited to point to the specific sections of the patent statute, patent rules and/or MPEP, as appropriate, which impose the requirement suggested above.

V.I. Objections to the Specification

A. Disclosure.

The disclosure has been objected to because it contains "an embedded hyperlink and/or other form of browser-executable code, such as on p. 44 and 85." According to the Examiner, "Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code." Office Action at 4.

Applicants respectfully traverse.

MPEP 608.01 states:

VII. Hyperlinks and Other Forms of Browser-Executable Code in the Specification

Examiners must review patent applications to make certain that hyperlinks and other forms of browser-executable code, especially commercial site URLs, are not included in a patent application. >37 CFR 1.57(d) states that an incorporation by reference by hyperlink or other form of browser executable code is not permitted.< Examples of a hyperlink or a browser-executable code are a URL placed between these symbols "<>" and http:// followed by a URL address. When a patent application with embedded hyperlinks and/or other forms of browser-executable code issues as a patent (or is published as a patent application publication) and the patent document is placed on the USPTO web page, when the patent document is retrieved and viewed via a web browser, the URL is interpreted as a valid HTML code and it becomes a live web link. When a user clicks on the link with a mouse, the user will be transferred to another web page identified by the URL, if it exists, which could be a commercial web site. USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites.

Applicants submit that the references to information are not embedded hyperlinks and/or other form of browser executable code. In order for the information to be an embedded hyperlink

or other form of browser executable code, there must be a field identifier (e.g. "<>") or the indicator "http://" followed immediately before the URL. Applicants submit that the URLs disclosed in the specification do not have the requisite identifiers or indicators to be recognized as a hyperlink or executed as code. Thus, when the text that the Examiner has objected to appears on the USPTO web page, it will not be interpreted as a valid HTML code and it will not become a live web link.

Applicants further submit that nothing in MPEP 608.01 prohibits citation of information from the internet in a form that will not create a live web link or is otherwise executable. MPEP 608.01 is not a prohibition against disclosure. It is a prohibition against certain *formats* that can be recognized by a computer as an instruction to perform a task or execute a command.

In the present application, the citation to information from the internet has been dissociated from the identifiers that would instruct a computer to perform a task or execute command. For example, on pg. 44 of the specification, URL has been represented in parentheses and separated from the indicator http:// (also in parentheses) by two words.

Accordingly, reconsideration and withdrawal of the objection to the specification is respectfully requested.

B. Abstract.

The abstract has been objected to because, according to the Examiner, "it does not properly describe the claimed invention, which is directed to a process." Office Action at 4.

Applicants respectfully traverse. Applicants submit that the Abstract clearly and accurately states the essence of the invention and indeed sets forth processes of the invention. Specifically, Applicants submit that the essence of the invention is the discovery of uses for ancestry information markers (AIMs). Particularly, “methods of using panels of the AIMs to draw an inference as to a trait of an individual” as recited in the Abstract of the disclosure.

Applicants further submit that neither a recitation of the steps of the methods of the invention nor further elaboration on the nature of the methods of the invention is applicable as the Abstract would necessarily exceed the length limitation set forth in MPEP 608.01(b)(C). Therefore, Applicants submit that the Abstract as filed complies with all required and suggested criteria, particularly within the confines of the conflicting directives provided in the MPEP.

Accordingly, reconsideration and withdrawal of the objection to the specification is respectfully requested.

IV. Rejections under 35 U.S.C. §112, First Paragraph (Enablement)

Claims 1, 3-5, 7-9, 24, 29-32, 38-45, and 47-58 have been rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly “does not reasonably provide enablement for a method wherein oligonucleotides do not detect SNPs.” Office Action at 5. The Examiner acknowledges, however, the specification is “enabling for a method wherein a SNP is detected by hybridizing a sample.” *Id.*

Independent claims 1 and 31, from which claims 3-5, 7-9, 24, 29-32, 38-45, and 47-5 ultimately depend, have been amended to clarify that nucleotide occurrences of SNPs are

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detected. Applicants submit that the rejection of claims 1, 3-5, 7-9, 24, 29-32, 38-45, and 47-58 is moot in view of the amendments to the independent claims.

Accordingly, withdrawal of rejection of claims 1, 3-5, 7-9, 24, 29-32, 38-45, and 47-58 under 35 U.S.C. §112, first paragraph is respectfully requested.

V. Rejections under 35 U.S.C. §112, Second Paragraph (Indefiniteness)

The Office Action states that "claims are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Office Action at 7.

Applicants note that it is not clear from this statement of the Office Action which claims are rejected. Clarification is respectfully requested. In subsequent paragraphs on pages 7-9, the Examiner elaborates specific claims and language that is allegedly indefinite. For the purposes of this response, those allegedly indefinite claims are addressed below.

1. "Wherein said contacting is performed under conditions suitable for detecting ..AIMs of the test individual by the hybridizing oligonucleotides."

According to the Examiner, the limitation "wherein said contacting is performed under conditions suitable for detecting AIMs of the test individual by the hybridizing oligonucleotides" is unclear, and therefore claims 1, 3-5, 7-9, 24, and 29-30 are indefinite. Office Action at 7.

Applicants submit that the indefiniteness rejection of claims 1, 3-5, 7-9, 24, and 29-30 is moot in view of the amendment to claim 1 which deletes the allegedly unclear phrase.

Accordingly, withdrawal of rejection of claims , 3-5, 7-9, 24, and 29-30 under 35 U.S.C. §112, first paragraph is respectfully requested.

2. "Thereby inferring a trait."

According to the Office Actions, "Claim 1 recites in the preamble 'a method of inferring.' Office Action at According to the Examiner, "the method does not comprise an active, positive step of 'inferring a trait.' The proviso after step (b) recites 'thereby inferring the trait.' Thus, it is not clear whether 'thereby inferring' is intended to be an active, positive step of inferring a trait, and therefore the relationship between the preamble and the method steps is unclear. As the intended limitation is not clear, claims 1, 3-5, 7-9, 24, and 29-30 are indefinite." Office Action at 8.

Applicants submit that the alleged infiniteness of claims 1, 3-5, 7-9, 24, and 29-30 is moot in view of the amendment to claim 1, which now specifies that the positive step b) of "identifying the population structure indicated by the nucleotide occurrences ... wherein the population structure infers the trait."

Accordingly, withdrawal of rejection of claims 1, 3-5, 7-9, 24, and 29-30 under 35 U.S.C. §112, first paragraph is respectfully requested.

3. "A population structure correlated with the trait"

The Office Action states "claim 1 recites a method of inferring a trait. The method further recites 'a population structure correlated with the trait' (line 7). Claim 1 also recites in line 13 'a

trait' and in line 14 'the trait.'" According to the Examiner, "[i]t is not clear whether a population structure recited in line 13 correlates with the same or a different trait then the trait recited in lines 1 and 7. It is also unclear whether "the trait of the individual" recited in line 14 is the trait recited in lines 1 and 7 or the trait recited in line 13 (if different). As the intended limitation is not clear, claims 1, 3-5, 7-9, 24, and 29-30 are indefinite.

Applicants submit that the alleged infiniteness of rejected claims is moot in view of the amendment to claim 1. Claim 1 has been amended with respect to the term "trait." The first occurrence of "trait," which is in the preamble, recites "a trait." The remaining references refer to "the trait." Thus, according to convention for antecedent basis of claim terms, each recitation of the "trait" in the steps of the method clearly refer to the same "trait." *See* MPEP 2173.05(e).

Accordingly, withdrawal of rejection of claims 1, 3-5, 7-9, 24, and 29-30 under 35 U.S.C. §112, first paragraph is respectfully requested.

4. "With a predetermined level of confidence "

According to the Examiner, it is not clear what the phrase "identifying, with a predetermined level of confidence" refers to in claims 1, 24, 31 and 45. Office Action at 8. Further, [a]s the intended limitation is not clear, claims 1, 3-5, 7-9, 24, 29-32, 38-45, and 47-58 are indefinite, according to the Examiner. *Id.*

Applicants submit that the indefiniteness rejection of claims 1, 3-5, 7-9, 24, 29-32, 38-45, and 47-58 is moot in view of the amendments thereto, which delete all the occurrences of the allegedly unclear phrase.

Accordingly, withdrawal of rejection of claims 1, 3-5, 7-9, 24, 29-32, 38-45, and 47-58 under 35 U.S.C. §112, first paragraph is respectfully requested.

5. "Thereby Estimating "

Claim 31 recites a method of estimating a trait comprising steps of contacting a sample with hybridizing oligonucleotides and identifying a population structure that correlates with AIMs in the test individual and the trait. The claim recites in step (a) "wherein said contacting is performed under conditions suitable for detecting ... AIMs of the test individual by the hybridizing oligonucleotides." It is not clear whether the method comprises actual, positive steps of hybridizing and detecting AIMs. The preamble recites "a method of estimating." However, the method does not comprise an active, positive step of "estimating a trait." The proviso after step (b) recites "thereby estimating the trait." Thus, it is not clear whether "thereby estimating" is intended to be an active, positive step of estimating a trait, and therefore the relationship between the preamble and the method steps is unclear. As the intended limitation is not clear, claims 31 - 32, 38-45, and 48-58 are indefinite." Office Action at 9.

Applicants submit that the alleged infiniteness of claims 31-32, 38-45, and 48-58 is moot in view of the amendment to claim 31, which specifies that the positive step b) of "identifying the population structure indicated by the nucleotide occurrences ... wherein the population structure estimates proportional ancestry."

Accordingly, withdrawal of rejection of claims 31-32, 38-45, and 48-58 under 35 U.S.C. § 112, second paragraph is respectfully requested.

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VI. Rejections under 35 U.S.C. § 103

Claims 1, 3-5, 7-9 and 30-32, 38-43, 45, 48, and 50-52 stand rejected under 35 U.S.C.

§103 as allegedly being obvious over the reference indicated below in sub-sections A-G, below.

To establish a prima facie case of obviousness, the Examiner must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. *See In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Second, the proposed modification of the prior art must have had a reasonable likelihood of success, determined from the vantage point of a skilled artisan at the time the invention was made. *See Amgen, Inc. v. Chugai Pharm. Co.*, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art reference or combination of references must teach or suggest all the limitations of the claims. *See In re Wilson*, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). It is well established that the teachings or suggestions, as well as the reasonable expectation of success, must come from the prior art, not from the applicant's disclosure. *See In re Vaeck*, 20 U.S.P.Q. 1438, 1442 (Fed. Cir. 1991).

Applicants submit that the 103 rejections do not fulfill any of the requirements set forth above, and therefore do not establish a prima facie case of obviousness.

For each of the obviousness rejection combinations below, the Examiner relies on NCBI submissions AC007172, AI619784 and/or AI300757. The Examiner admits that none of the

remaining references cited for methodology teach or suggest the elected species of SEQ ID NO:70.

Applicants submit that none of AC007172, AI619784 or AI300757 teach the species of SEQ ID NO:70. SEQ ID NO:70 recites a nucleotide sequence containing a single nucleotide polymorphism (SNP) at nucleotide position 50. The sequence disclosed in SEQ ID NO:70 indicates by using the symbol "s" that the nucleotide at position 50 can be either a G or a C nucleotide. Moreover, the designation "SNP" indicates that the each of the two polymorphic nucleotide forms is present at a level in the population sufficient to establish the occurrence as a polymorphism rather than a simple random mutation, as is well known in the art. None of the sequences cited by the Examiner teach or suggest this limitation of the invention. Each sequence represents a single nucleotide sequence with no polymorphic positions identified. Applicants submit that the mere presence of the base sequence in the prior art, without disclosure of the single nucleotide polymorphism at position 50 of SEQ ID NO: 70, does not establish the full scope of the limitation encompassed by SEQ ID NO:70. Indeed, there is no indication in the sequences cited by the Examiner that the nucleotide corresponding to position 50 of SEQ ID NO:70 is present in any more than a single nucleic acid sample, much less in at least 1% of the population as required for a SNP. Applicants submit that a single nucleotide sequence - with no degeneracy or variation - does not teach or suggest a SNP.

Furthermore, Applicants acknowledge in the specification that the SNPs of the present invention are not novel. They were culled from publicly available databases, and thus are not, in

and of themselves, novel. *See* Specification at p. 82-3, [0189]. However, the SNPs of claims 1, 3-5, 7-9 and 30-32, 38-43, 45, 48, and 50-52 are further required by the claims to be ancestry informative markers or AIMS. The specification teaches that only a small percentage of SNPs that have been identified are even good “candidate” AIMS. Moreover, only half of the candidate AIMS turn out to be useful, validated AIMS for the purposes of the invention. *See* specification p. 83, [0190].

Not only do the sequences cited by the Examiner fail to disclose that the sequences contain a variation that represents a true polymorphism corresponding to position 50 of SEQ ID NO:70, but (as discussed further below) there would have been no reasonable expectation of success that any individual SNP disclosed in the art would satisfy the requirements of an AIM. *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) (“The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art.”).

Finally, there is no suggestion or teaching in either the cited sequences or the references cited for methodology (below), to use the AIM of SEQ ID NO:70 to arrive at the claimed method. The Examiner alleges that “the motivation would have been to facilitate detection of ancestral proportions in human.” However, the motivation required to establish obviousness must be a specific motivation taught by the references themselves to make the specific combination with SEQ ID NO:70, not the general motivation the Examiner suggests. As the

Federal Circuit has explained, “[t]here must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination.” *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992).

Put another way, it may have been obvious to try every possible SNP in the human genome, but obvious to try is not the standard under § 103. “The admonition that ‘obvious-to-try’ is not the standard under § 103 has been directed mainly at two kinds of error”

i) “In some cases, what would have been ‘obvious-to-try’ would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of the many possible choices is likely to be successful.”

ii) “In others, what was ‘obvious-to-try’ was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.” *In re O’Farrell*, 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).]

Given that the human haploid genome has roughly 3.9×10^9 individual nucleotide positions, that only a fraction of these are polymorphic, and that only a fraction of the polymorphisms qualify as AIMs of the invention, a general motivation to facilitate detection of ancestral proportions falls far short of specifically suggesting that the SNP of SEQ ID NO:70 should be combined to this end. Only if multi-millions of possible permutations were attempted would the method of the present invention based on detecting *inter alia* SEQ ID NO:70 result.

Absent the teachings of the present application (that SEQ ID NO:70 describes a SNP that is also an ancestry informative marker), combining the cited sequences in a method for inferring a trait is nothing more than impermissible hindsight.

On this basis alone, the Examiner has failed to satisfy the requirements for prima facie obviousness of claims 1, 3-5, 7-9, 24, 30-32, 38, 40-43, 45 and 50-52. For thoroughness and to be completely responsive, however, applicants will briefly point out the shortcomings of the additional references cited in the Office Action.

A. McKeigue in view of Birren and Collins-Schramm

Claims 1, 3-5, and 31 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over McKeigue, *Ann. Hum. Genet.*, 64:171-186 (2000), in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submission, ID number AI300757 (2/01/1999); and further in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002). Office Action at p. 9.

Applicants respectfully traverse:

For the reasons stated above, the combination does not teach or suggest the SNP of SEQ ID NO:70. Furthermore, neither McKeigue nor Collins-Schram teach or suggest that SNPs which are not in genes linked to the trait (i.e., biogeographical ancestry as elected in response to the restriction requirement) can be used to detect a population structure the can then be used to infer a trait. The markers detected by McKeigue are in genes that have “large differentials in

West African s and European.” See McKeigue, *supra*, at 174. Thus, they are in genes linked to the trait of biogeographical ancestry.

Collins-Schram does not detect SNPs at all. Instead, that cited reference teaches a method for screening dinucleotide insertion/deletion and microsatellite polymorphisms. The skilled artisan would appreciate that dinucleotide insertion/deletion and microsatellite polymorphisms are very different from SNPs because they are characterized by a more complex allelic structure, and thus, a much lower effective population size.

Prior to present invention, it had not been shown that markers such as SNPs (with large effective population sizes), located outside of genes, could be used to estimate admixture accurately (as evidenced by the demonstration of correlation with anthropometric phenotypes like iris color), or to resolve sub-populations. The use of SNPs for this purpose is key since SNPs are conveniently and economically measured, unlike dinucleotide insertion/deletion and microsatellite polymorphisms which are cumbersome and expensive to measure.

Neither neither McKeigue nor Collins-Schram teach or suggest these key limitations of . Furthermore, there is no suggestion in the references themselves to combine the references and arrive at the claimed invention containing these limitations. Thus, the Examiner has failed to meet his burden of establishing the obviousness of claims 1, 3-5, and 31 in view of the suggested combination.

Accordingly, withdrawal of rejection of claims 1, 3-5, and 31 under 35 U.S.C. §103 is respectfully requested.

B. Parra in view of Birren and Collins-Schramm

Claims 1, 3-5, 31, and 39 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Parra, *Am. J. Physical Antropol*, 114-118 (2001), in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submission, ID number AI300757 (2/01/1999); and further in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002). Office Action at p. 11.

Applicants respectfully traverse.

Para describes *self-reported* sub-population affiliation, such as “South Carolina” or “Gullah”. These are social constructs of population affiliation much like those used to identify the parental populations “African” or “European”, not phenotypes or physical traits, as recited in claim 1. Although Parra and others have shown association between admixture and social constructs of identity including geographical origin, the methods of the present invention are the first based on the association between population structure and an actual *phenotype* (trait). Furthermore, the 10 autosomal SNPs of Parra were located within genes linked to a trait, rather than outside of coding sequences linked to a trait. Neither Collins-Schramm’s dinucleotide insertion/deletion and microsatellite polymorphisms screening nor the sequences of Birren compensate for the deficiencies of Parra. Similarly, as discussed above in section VI.A, neither Collins-Schramm nor Parra teach or suggest using SEQ ID NO:70 to arrive at a method to infer or estimate a trait as required by the independent claims. Thus, the combination suggested fails to establish prima facie obviousness because it does not teach or suggest all the limitations of the

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claims, does not provide the requisite motivation to combine with a reasonable probability of success.

Accordingly, withdrawal of rejection of claims 1, 3-5, 31, and 39 under 35 U.S.C. §103 is respectfully requested.

C. Sorenson in view of Birren and Collins-Schramm

Claims 1, 3-5, 24, 30-31, 45, and 50-52 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Sorenson, US 2003/0172065, in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submission, ID number AI300757 (2/01/1999); and further in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002). Office Action at p. 12.

Applicants submit that Sorenson, which was published on September 11, 2003 is not a proper prior art reference for the present application, which was filed on August 19, 2003 and entitled to an even earlier priority at described above. As a U.S. patent *application*, Sorenson can only be used as publication as of its publication date. Thus, the rejection of claims 1, 3-5, 24, 30-31, 45, and 50-52 based on a combination of references including Sorenson is improper.

Furthermore, for the reasons stated above, the combination does not teach or suggest SEQ ID NO:70, and therefore does not establish a prima facie case of obviousness.

Accordingly, withdrawal of rejection of claims 1, 3-5, 24, 30-31, 45, and 50-52 under 35 U.S.C. § 103, first paragraph is respectfully requested.

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D. Sorenson in view of Birren and Collins-Schramm, and further in view of Hanis

Claims 7-8, 32, and 38 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Sorenson, US 2003/0172065, in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submission, ID number AI300757 (2/01/1999); in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002), as applied to claims 1, 3-5, 24, 30-31, 45, and 50-52, and further in view of Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986). Office Action at p. 13.

Applicants submit that Sorenson, which was published on September 11, 2003 is not a proper prior art reference for the present application, which was filed on August 19, 2003 and entitled to an even earlier priority at described above. As a U.S. patent *application*, Sorenson can only be used as publication as of its publication date. Thus, the rejection of claims 7-8, 32, and 38 based on a combination of references including Sorenson is improper.

Furthermore, for the reasons stated above, the combination does not teach or suggest SEQ ID NO:70, and therefore does not establish a prima facie case of obviousness.

Accordingly, withdrawal of rejection of claims 7-8, 32, and 38 under 35 U.S.C. § 103, first paragraph is respectfully requested.

E. Sorenson in view of Birren and Collins-Schramm, and further in view of Kanetsky

Claim 9 has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sorenson, US 2003/0172065, in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submission, ID

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number AI300757 (2/01/1999); in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002), as applied to claims 1, 3-5, 24, 30-31, 45, and 50-52, and further in view of Kanetsky, *Am. J. Hum. Genet.*, 70:770-775 (2/6/2002). Office Action at p. 14.

Applicants submit that Sorenson, which was published on September 11, 2003 is not a proper prior art reference for the present application, which was filed on August 19, 2003 and entitled to an even earlier priority at described above. As a U.S. patent *application*, Sorenson can only be used as publication as of its publication date. Thus, the rejection of claim 9 based on a combination of references including Sorenson is improper.

Furthermore, for the reasons stated above, the combination does not teach or suggest SEQ ID NO:70, and therefore does not establish a prima facie case of obviousness.

Accordingly, withdrawal of rejection of claim 9 under 35 U.S.C. § 103, first paragraph is respectfully requested.

F. Sorenson in view of Birren and Collins-Schramm, and further in view of Akey.

Claim 29 has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sorenson, US 2003/0172065, in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submission, ID number AI300757 (2/01/1999); in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002), as applied to claims 1, 3-5,24, 30-31,45, and 50-52, and further in view of Akey, *BioTechnique*, 30(2):358-367 (2001). Office Action at p. 15.

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Applicants submit that Sorenson, which was published on September 11, 2003 is not a proper prior art reference for the present application, which was filed on August 19, 2003 and entitled to an even earlier priority at described above. As a U.S. patent *application*, Sorenson can only be used as publication as of its publication date. Thus, the rejection of claim 29 based on a combination of references including Sorenson is improper.

Furthermore, for the reasons stated above, the combination does not teach or suggest SEQ ID NO:70, and therefore does not establish a prima facie case of obviousness.

Accordingly, withdrawal of rejection of claim 29 under 35 U.S.C. § 103, first paragraph is respectfully requested.

G. Parra in view of Birren and Collins-Schramm, and further in view of Pritchard

Claims 40-43 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over of Parra, *Am. J. Physical Antropol.*, 114-118 (2001), in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submissions ID number AI300757 (2/01/1999); in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002), as applied to claims 1, 3, 31, and 39, and further in view of Pritchard, *Theoretical Population Biology*, 60:227-237 (2001). Office Action at p. 16.

Applicants submit that Sorenson, which was published on September 11, 2003 is not a proper prior art reference for the present application, which was filed on August 19, 2003 and entitled to an even earlier priority at described above. As a U.S. patent *application*, Sorenson

can only be used as publication as of its publication date. Thus, the rejection of claims 40-43 based on a combination of references including Sorenson is improper.

Furthermore, for the reasons stated above, the combination does not teach or suggest SEQ ID NO:70, and therefore does not establish a prima facie case of obviousness.

Accordingly, withdrawal of rejection of claims 40-43 under 35 U.S.C. § 103, first paragraph is respectfully requested.

G. Sorenson in view of Birren and Collins-Schramm, and further in view of Pritchard

Claim 48 has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sorenson, US 2003/0172065, in view of Birren, NCBI submission, ID number AC007172, (5/01/1999); or NCBI submission, ID number AI619784 (3/07/2000); or NCBI submission, ID number AI300757 (2/01/1999); in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002), as applied to claims 1, 3-5, 24, 30-31, 45, and 50-52, and further in view of Pritchard, Pritchard, *Genetics*, 155:945-959 (2000). Office Action at p. 17.

Applicants submit that Sorenson, which was published on September 11, 2003 is not a proper prior art reference for the present application, which was filed on August 19, 2003 and entitled to an even earlier priority at described above. As a U.S. patent *application*, Sorenson can only be used as publication as of its publication date. Thus, the rejection of claim 48 based on a combination of references including Sorenson is improper.

Furthermore, for the reasons stated above, the combination does not teach or suggest SEQ ID NO:70, and therefore does not establish a prima facie case of obviousness.

Accordingly, withdrawal of rejection of claims 48 under 35 U.S.C. § 103, first paragraph is respectfully requested.

H. Indicia of Non-Obviousness

Having rebutted the Examiner's prima facie case of obviousness, Applicants are under no obligation to provide evidence of non-obviousness. In an effort to expedite prosecution, however, Applicants provide the following comments regarding additional objective indicia of non-obviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966); *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538, 218 USPQ 871, 879 (Fed. Cir. 1983) ("evidence rising out of the so-called 'secondary considerations' must always when present be considered en route to a determination of obviousness.")

The methodology claimed in the present application has been subject to significant discussion in both lay and technical publications. This is in part due to the celebrated **commercial success** of the invention, particularly when DNAPrint Genomics, owner and developer of the methods, helped to solve the well-publicized Louisiana serial killer case using the claimed technology. *See* Touchette, "Genome Test Nets Suspected Serial Killer" (Attached hereto as Exhibit A); Ritter, "DNA test in La. killings is said to have indicated attacker's race" (Attached hereto as Exhibit B). Attached hereto as Exhibit C is one such commentary on the technology of the present invention by Cho and Sankar (*Nature Genetics Supp.* S8-S11, 2004) that further describes the **long-felt-need** for methods that accurately determine biogeographical ancestry and shortcomings of the art (**failure of others**) in achieving this objective. This

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reference is clearly critical of the methods of the present invention in part because of ethical concerns, but also because their view as skilled artisans was that methods for accomplishing the end result of the present invention were not available. This reference establishes the view through publication in a prestigious peer-reviewed journal, that many though the weight of evidence actually taught away from the present invention. Thus, it can clearly be considered an unexpected result that the present invention has been found to be highly successful, as described in the accompanying response co-authored by inventors Shiver and Frudakis along with Budowle (Nature Genetics 37:449-50, 2005; attached hereto as Exhibit D), and as taught by the present specification.

In view of the above-described objective evidence of non-obviousness, Applicants submit that the claimed methods were not obvious over the prior art.

Accordingly, withdrawal of rejection of claims 1, 3-5, 7-9, 24, 29, 30-32, 38-39, 40-43, 45, 48 and 50-52 under 35 U.S.C. § 103, first paragraph is respectfully requested.

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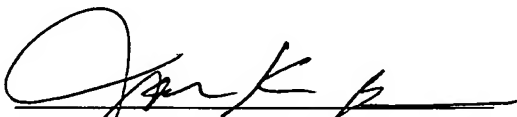
Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

A check in the total amount of \$690.00 is enclosed as payment of the three-month Extension of Time fee (\$510.00) and for the Information Disclosure Statement (\$180.00). No other fee is believed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees that are required, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

Date: August 14, 2006



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